Remarks

Applicant thanks the Examiner for his detailed recitation of the reasoning behind the rejections, and respectfully requests reconsideration of the claim rejections.

This amendment is filed as a submission for the Request for Continued Examination previously filed on December 15, 2004. Applicant petitions for a three month extension of time.

Claims 29, 34 and 49 are pending for examination with claim 29 being the only independent claim and claim 34 being withdrawn. No new matter has been added.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claim 33 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification. Applicant respectfully requests reconsideration and withdrawal of the rejection.

Claim 29 includes compounds that decrease calcium influx of neuronal cells caused by aggregated β-amyloid (Aβ) protein degradation products. Among the compounds provided in the specification are non-NMDA channel antagonists. Non-NMDA channel antagonists are a class of compounds recognized in the art. Applicant further provided a description of a number of this class of compounds in the specification. Additional compounds described in the application are $MgCl_2$, and decoy peptides.

The requirement for an adequate written description provides that the specification disclose the invention sufficiently such that the applicant conveys to one of ordinary skill in the art that the applicant was in possession of the invention as claimed. Vas-Cath v. Mahurkar, 35 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991) (written description requirement requires that the claimed invention must be described clearly enough to allow one of ordinary skill in the art to recognize that the inventors invented the claimed invention). Applicant in this case has done so. The term "compounds that decrease calcium influx of neuronal cells caused by aggregated β-amyloid (Aβ) protein degradation products", particularly in combination with the description of specific compounds provided in the specification, is more than adequate to convey to the skilled person that Applicant was in possession of the invention.

The Examiner cites the University of California v. Eli Lilly case for the proposition that the written description of a genus of cDNAs requires either disclosure of a representative number

of cDNAs or a recitation of structural features common to the members of the genus. (Office Action at page 4.) The Examiner concludes on page 5 of the Office Action that the specification does not satisfy either of the Lilly criteria.

Applicant respectfully disagrees. First, the Lilly criteria are pertinent to the description of cDNAs, more particularly a genus of unknown cDNAs. In the present case, the claim element at issue is not a genus of cDNAs, but rather is compounds that decrease calcium influx of neuronal cells caused by aggregated β-amyloid (Aβ) protein degradation products, which includes known classes of compounds, i.e., the decoy peptides and the non-NMDA channel antagonists. Second, the person of skill in the art can readily envision, based on the description in the specification, the invention now claimed, because decoy peptides and the non-NMDA channel antagonists are well known in the art. For example, the term non-NMDA channel antagonists is analogous to describing a class of non-steroidal anti-inflammatory drugs (NSAIDs) – the person of skill in the art immediately recognizes these compounds as a class. Third, the case law does not require that a description of the structure of compounds be provided in the manner suggested by the Examiner. Applicant notes that the case law cited by the Examiner states that a description of a genus of cDNAs or other compounds "may" or "can" be achieved by description of structure or by providing a representative number of compounds. However, Applicant is not aware of any case law that stands for the proposition that description of structure or providing a representative number of compounds is the only way to provide an adequate written description. Therefore, based on the description in the specification, Applicant has conveyed possession of the claimed invention to one of ordinary skill in the art.

Accordingly, Applicant's specification provides an adequate written description of claim 29 as presently amended. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph therefore is requested.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claim 29 under 35 U.S.C. § 103(a) as unpatentable over Buxbaum (US 5,385,915), alone and further in view of Ingram, et al. (US 2003/0114510A1) as evidence of inherency; and Sharpe, et al. (US 6,552,066) as applied to claim 29, and further in view of Ingram (WO 98/30229). Applicant respectfully traverses the rejection.

First, the Examiner suggests that the teaching of glutamate by Buxbaum (e.g., in claim 10) in a long list of modulators of protein phosphatases is a teaching of a compound that decreases neuronal calcium influx as recited in the previously pending claims. Applicant respectfully disagrees. Applicant's specification teaches the opposite is true. On page 1, lines 22-25, the specification states: "The work of Mattson et al. (*J. Neurosci.* 12:376-389, 1992) indicates that β-amyloid peptides, including the sequence Aβ25-35, in the presence of the excitatory neurotransmitter glutamate causes an immediate increase in intracellular calcium...." On page 16, lines 5-7, Applicant's specification teaches that non-NMDA channels, which increase internal calcium concentrations, are ordinarily activated by a combination of two factors, one of which is the presence of the excitatory amino acid neurotransmitter glutamate. Thus, glutamate results in an increase in calcium, and accordingly glutamate cannot be a compound that decreases neuronal calcium influx as recited in the claims. There is nothing in Buxbaum that teaches that glutamate is a compound that decreases neuronal calcium influx. Thus Buxbaum does not teach or suggest the second element of the claimed invention.

The Examiner suggests that the Ingram published application (US 2003/0114510A1) "discloses that non-NMDA channel antagonists, such as 'glutamate' inherently '*decrease neuronal calcium influx by beta amyloid protein degradation products*'." (Office Action at page 9, emphasis in original). The Ingram reference is, of course, the publication of the instant US application. The Examiner has not provided a citation to the section of Ingram that states the alleged effect of glutamate in decreasing calcium influx. As noted above, Applicant's specification teaches the opposite effect of glutamate. Thus it is not clear what the source of the Examiner's assertion is.

Second, the Examiner admits that the Buxbaum patent does not teach the first element of the claimed invention, DAPH. Instead, Buxbaum teaches the use of a variety of "kinase modulators", including the kinase inhibitor tyrphostin. The Examiner suggests the Sharpe patent teaches tyrphostin is an equivalent of DAPH. Even assuming this is true (and that there are no contrary recitations in the art), Buxbaum also teaches that kinase modulators can include "compounds increasing intracellular calcium" (col. 11, line 31), which is directly contrary to the effect of Applicants invention. Therefore, Buxbaum's teachings are of limited relevance, if any, to the DAPH element of Applicant's claims.

Third, the Buxbaum patent teaches to administer at least one "modulator of protein kinase or phosphatase" (e.g., in claim 1) for controlling the processing of amyloid precursor protein. Buxbaum teaches that the compounds listed in the patent are used to "affect or modulate the phosphorylation state of proteins … by inhibiting or stimulating the activity of kinases … or by inhibiting or stimulating phosphatases." (Col. 11, lines 3-7, emphasis added).

The net effect of the teachings of the Buxbaum patent is that one of ordinary skill in the art would not be led specifically to combine DAPH and a compound that decreases calcium influx of neuronal cells as is taught by Applicant. To the contrary, Buxbaum does not combine two classes of "modulators", particularly not the two types of molecules claims in combination by Applicant.

Moreover, even assuming that Sharpe does teach an equivalence between tyrphostin and DAPH, there is nothing in the combination of Buxbaum and Sharpe that suggests that DAPH is somehow to be selected from all of the possible equivalents of DAPH and combined with a compound that decreases calcium influx of neuronal cells. Simply put, the combination of the cited references does not provide the requisite specific teaching to one of ordinary skill in the art to make the claimed combination.

The Examiner suggests that In re Fout supports the rejection because that case states that obviousness based on functional equivalency does not require an express suggestion to substitute an equivalent. Applicant does not necessarily disagree with the statement of the law, but does disagree that there is sufficient suggestion in the combination of Buxbaum and Sharpe to provide the requisite motivation to substitute DAPH for tyrphostin. If taken to its logical conclusion, substitutions of the type suggested by the Examiner would permit substitution of any tyrosine kinase inhibitor so long as some reference teaches functional equivalency. What is unclear is how one of ordinary skill in the art would be expected to select the specific claimed compound from among the potentially vast genus of equivalents, given that Buxbaum (or Sharpe) does not provide any guidance to making such a selection.

Moreover, MPEP section 2144.06 acknowledges that the case law provides that suggesting equivalence is not the end of the analysis required for obviousness. This section of the MPEP states that "in order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical

equivalents." MPEP 2144.06 (emphasis added), citing In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components).

Therefore, the Buxbaum patent, as interpreted in view of the Sharpe patent and the Ingram publication, is insufficient to support the obviousness rejection as asserted by the Examiner.

The Examiner also rejected claims 29 and 49 over the combination of Buxbaum, as interpreted in view of the Sharpe patent and the Ingram publication, and the Ingram PCT application (WO 98/30229).

First, all of the reasons stated above in response to the rejection of claim 29 are reiterated and apply equally to this rejection.

Second, the Examiner states that one of ordinary skill in the art would have motivated to add Ingram's decoy peptides into Buxbaum's compositions because (1) Buxbaum teaches incorporation of calcium channel modulating compounds (glutamate), and (2) the Buxbaum and the Ingram compositions are for the same purpose, treatment of Alzheimer's disease. (Office Action at page 11). The Examiner also cited to In re Kerkhoven. The flaw in this rejection is that Buxbaum and Ingram teach opposite effects to treat the same disease. In particular, while Buxbaum suggests using glutamate, Ingram teaches that glutamate results in calcium influx (e.g., page 1, lines 18-20), which the instant application teaches would exacerbate the disease.

Buxbaum also does not provide the specific motivation to combine the two kinds of compounds claimed by Applicant. The Examiner states that "any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. (Office Action at p. 16). Applicant agrees that In re McLaughlin is properly cited for its teaching that only knowledge known to one of ordinary skill in the art at the time the invention was made is correctly used in a determination of obviousness. However, the Federal Circuit has amplified and refined the warnings against the insidiousness of hindsight reasoning. The court has repeatedly warned of the need for specificity. For example, in In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) the court stated that "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed". In In re Rouffet, 149 F.3d 1350, 1359, 47

USPQ2d 1453, 1459 (Fed. Cir. 1998) the court stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination".

In view of these (and other decisions), Applicant objects to the use of hindsight reasoning in the Examiner's selection of DAPH as an equivalent of tyrphostin and its combination with compounds that decrease calcium influx of neuronal cells. The claimed combination is not obvious from the combination of references cited by the Examiner, as noted above, without resorting to the teachings in Applicant's specification.

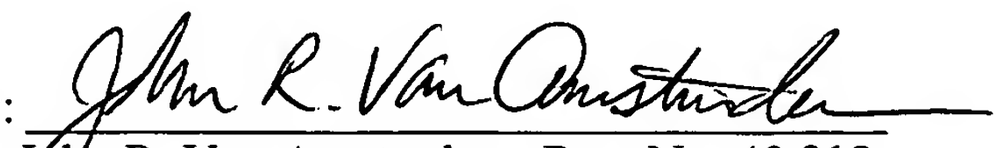
Accordingly, Applicant respectfully requests that the rejection of claims 29 and 49 as being unpatentable under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

Applicant respectfully requests reconsideration of the claims in view of the amendments and reasoned statements made above. If the Examiner wishes to expedite the prosecution, or if the amendment is defective or unclear, then the Examiner is invited to telephone the undersigned at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Vernon M. Ingram et al., Applicant

By: 

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